

Old Claim No.	Previous Status	Proposed New Claim No.
88	allowed	179
89	allowed	182
90	allowed	185-187
94	allowed	192
117		178
118	allowed	179
119	allowed	178
120	allowed	178
121		178
122		179
123		181
124	allowed	180
126		182-184
127		185-187
128		188-190
129		188-190
130		188-190
131		188-190
132		188-190
133		191
134		194
135	allowed	195
137	allowed	None
138	allowed	185-187
139	allowed	188
140	allowed	188
142	allowed	191-193
143		198-200
144		201-203
145		201-203
146		201-203

Old Claim No.	Previous Status	Proposed New Claim No.
147		201-203
148		204
149		198-200
150	allowed	206
151	allowed	210
152	allowed	206
153		206
154	allowed	207
155	allowed	209
156	allowed	None
157	allowed	208
158	cancel	
159	allowed	195
160	allowed	195
165	allowed	206
166	allowed	207
167	allowed	208
168	allowed	209
169	allowed	None
170	allowed	None
171	allowed	None
172		None
173		None
174		None
175	allowed	212
176	allowed	212-213
177	allowed	198-200

Please cancel claims 88-90, 94, 117-135, 137-140, 142-160, 165-177, without prejudice, and replace them with the new claims provided below.

178. A purified and isolated nucleic acid encoding a glial cell line-derived neurotrophic factor (GDNF) polypeptide, wherein said nucleic acid:

- (a) comprises nucleotides 304 through 705 of SEQ ID NO:3; or
- (b) comprises nucleotides 105 through 506 of SEQ ID NO:5; or
- (c) encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:4; or
- (d) encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:6; or
- (e) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding the polypeptide of SEQ ID NO:6 under hybridization conditions comprising 6X SSPE and 0.1% SDS at 50°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C and wherein said polypeptide promotes dopamine uptake in dopaminergic neurons; or
- (f) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding amino acids 2 to 86 of SEQ ID NO:4 under hybridization conditions comprising 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C and wherein said polypeptide promotes dopamine uptake in dopaminergic neurons.

179. The nucleic acid of claim 178 wherein said nucleic acid additionally encodes for an amino-terminal methionine residue when said GDNF polypeptide is recombinantly produced by a bacterial expression system.

180. A purified and isolated nucleic acid encoding a polypeptide comprising the GDNF polypeptide set forth in SEQ ID NO:27 or SEQ ID NO:28.

181. A purified and isolated nucleic acid comprising a nucleic acid fully complementary to the nucleic acid of claim 178, 179, or 180.

182. An expression vector comprising the nucleic acid of claim 178.

183. An expression vector comprising the nucleic acid of claim 179.

184. An expression vector comprising the nucleic acid of claim 180.

~~185. An isolated host cell comprising the expression vector of claim 182.~~

186. An isolated host cell comprising the expression vector of claim 183.

187. An isolated host cell comprising the expression vector of claim 184.

188. The host cell of claim 185 wherein said cell is selected from the group consisting of :

- (a) a microorganism;
- (b) an animal cell;
- (c) a COS cell;
- (d) a bacterial cell; and
- (e) *E. coli*.

189. The host cell of claim 186 wherein said cell is selected from the group consisting of :

- (a) a bacterial cell; and
- (b) *E. coli*.

190. The host cell of claim 187 wherein said cell is selected from the group consisting of :

- (a) a microorganism;
- (b) an animal cell;
- (c) a COS cell;
- (d) a bacterial cell; and
- (e) *E. coli*.

191. The host cell according to claim 188, 189, or 190 wherein said cell is transformed or transfected *ex vivo*.
192. The host cell of claim 191 wherein said cell produces said GDNF polypeptide.
193. The host cell according to claim 192 wherein said cell secretes said GDNF polypeptide.
194. The host cell according to claim 193 wherein said cell is a cell suitable for human implantation.
195. An isolated host cell which expresses a nucleic acid encoding a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons, wherein said nucleic acid is operatively linked to a non-native promoter in an expression vector and wherein said nucleic acid:
 - (a) comprises nucleotides 304 through 705 of SEQ ID NO:3; or
 - (b) comprises nucleotides 105 through 506 of SEQ ID NO:5; or
 - (c) encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:4; or
 - (d) encodes a polypeptide comprising the amino acid sequence set forth in SEQ ID NO:6; or
 - (e) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding the polypeptide of SEQ ID NO:6 under hybridization conditions comprising 6X SSPE and 0.1% SDS at 50°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C; or
 - (f) hybridizes to an oligonucleotide probe fully complementary to a nucleic acid encoding amino acids 2 to 86 of SEQ ID NO:4 under hybridization conditions comprising 6X SSPE, 0.1% SDS and 30% formamide at 42°C, followed by washing in 2X SSPE and 0.1% SDS at room temperature and twice in 0.1x SSPE, 0.1% SDS preheated to 50°C.
196. An isolated host cell which expresses a nucleic acid encoding a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons, wherein said nucleic acid is operatively

linked to a non-native promoter in an expression vector and wherein said nucleic acid encodes a polypeptide comprising the GDNF polypeptide set forth in SEQ ID NO:27 or SEQ ID NO:28.

198. A method for the production of a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons comprising the steps of:

- (a) culturing a host cell transformed or transfected with the vector of claim 182 under conditions suitable for the expression of said GDNF polypeptide; and optionally
- (b) isolating said GDNF polypeptide produced by said cell.

199. A method for the production of a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons comprising the steps of:

- (a) culturing a host cell transformed or transfected with the vector of claim 183 under conditions suitable for the expression of said GDNF polypeptide; and optionally
- (b) isolating said GDNF polypeptide produced by said cell.

200. A method for the production of a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons comprising the steps of:

- (a) culturing a host cell transformed or transfected with the vector of claim 184 under conditions suitable for the expression of said GDNF polypeptide; and optionally
- (b) isolating said GDNF polypeptide produced by said cell.

201. The method according to claim 198 wherein said cell is selected from the group consisting of:

- (a) a microorganism;
- (b) an animal cell;
- (c) a COS cell;
- (d) a bacterial cell; and
- (e) *E. coli*.

202. The method according to claim 199 wherein said cell is selected from the group consisting of:

- (a) a bacterial cell; and
- (b) *E. coli*.

203. The method according to claim 200 wherein said cell is selected from the group consisting of:

- (a) a microorganism;
- (b) an animal cell; and
- (c) a COS cell; and
- (d) a bacterial cell; and
- (e) *E. coli*.

204. The method according to claim 201, 202, or 203 further comprising a step of refolding said GDNF polypeptide.

205. The method according to claim 204 further comprising a step of refolding said GDNF polypeptide to form a disulfide-bonded dimer.

206. A method for the production of a GDNF polypeptide that promotes dopamine uptake in dopaminergic neurons comprising the steps of:

- (a) culturing the transformed or transfected host cell of claim 195 under conditions suitable for the expression of said GDNF polypeptide; and
- (b) isolating said GDNF polypeptide produced in a substantially purified form from said host cell culture.

207. The method according to claim 206 wherein said host cell is selected from the group consisting of :

- (a) a microorganism;
- (b) an animal cell;
- (c) a COS cell;
- (d) a bacterial cell; and
- (e) *E. coli*.